UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

CIVIL ACTION NO.: 1:11-cv-10204-MLW

ROBERT ZEMAN

and

JULIA ZEMAN,

Plaintiffs,

v.

ZIV WILLIAMS, M.D.,

EMAD ESKANDAR, M.D.,

INDIVIDUAL MEMBERS OF THE INSTITUTIONAL REVIEW BOARD: MELISSA FRUMIN, M.D., HINA ALAM, SARY F. ARANKI, M.D., RHONDA BENTLEY-LEWIS, M.D., SUSAN BURNSIDE, RICHARD D'AUGUSTA, ASHWIN DHARMADHIKARI, M.D., DAVID A. JONES, M.D., DEBORAH ECKER, ROBERT J. GLYNN., ELIZABETH L. HOHMANN, M.D., THOMAS KOLOKOTRONES, KEITH A. MARCOTTE, FRANCISCO MARTY. M.D., ELINOR A MODY, M.D., JOAN RILEY, ANDREW P. SELWYN, ARTHUR C. WALTMAN, M.D., SJIRK WESTRA, M.D. and SEAN R. WILSON, M.D.,

MEDTRONIC, INC.,

and

NEUROLOGIX, INC.,

Defendants.

PLAINTIFFS' MEMORANDUM OF LAW IN OPPOSITION TO DEFENDANT NEUROLOGIX, INC.'S MOTION TO DISMISS

INTRODUCTION

Plaintiffs Robert Zeman and Julia Zeman (collectively, "Plaintiffs"), by and through their attorneys, Alan C. Milstein of Sherman, Silverstein, Kohl, Rose & Podolsky, P.A. and Scott Charnas of Charnas Law Firm, P.C.,[1] respectfully submit this memorandum of law in opposition to the motion to dismiss ("Motion") filed on behalf of Defendant Neurologix, Inc. ("Neurologix"). As the Plaintiffs have stated claims against Neurologix for negligence, products liability negligence, and breach of implied warranty, the Motion must be denied.[2]

STATEMENT OF THE FACTS

I.

In February 1996, at the age of thirty, Mr. Zeman was diagnosed with young-onset Parkinson's disease.[3] By November 2008, the effects of the medications Mr. Zeman was taking to control his symptoms were wearing off faster and faster.[4] Mr. Zeman began researching various treatment options, including Deep Brain Stimulation, one of the latest FDA-approved treatments for Parkinson's.[5] Mr. Zeman declined this treatment for multiple reasons, including the need for multiple surgeries and constant adjustments.[6] Subsequently, Mr. Zeman learned about a clinical trial being conducted at Massachusetts General Hospital ("experiment") using Gene Transfer on both sides of the brain in the subthalamic nucleus ("STN").[7]

Gene Transfer, sometimes mistakenly called Gene Therapy, is an experimental procedure whereby genes are directed to target a region of the body using a viral vector, on the theory that

---

[1] A motion to admit Mr. Milstein *pro hac vice* will be forthcoming. This pleading is signed by Mr. Charnas.

[2] Furthermore, the Plaintiffs will shortly move to file a Second Amended Complaint adding additional allegations against Neurologix. Thus, even if this Court is in agreement with Neurologix' arguments, Neurologix should not be dismissed from this case.

[3] See Amended Complaint, ¶ 15.

[4] See Amended Complaint, ¶ 17.

[5] See Amended Complaint, ¶ 18.

[6] See Amended Complaint, ¶ 18.

[7] See Amended Complaint, ¶ 19.

the genes will express themselves, thereby creating healthy genes in the part of the body where defective genes had resided.[8] Here, the viral vector was the adeno-associated virus ("AAV").[9]

The design of the experiment was as follows: genes would be delivered directly into both sides of the brain in the hope that they would produce an enzyme that would result in the increased production of gamma-aminobutyric acid, a neurotransmitter in short supply in the brains of Parkinson's patients.[10] The experiment was a single-blind placebo study, meaning that half the subjects would undergo a "sham surgery" where no agent was delivered, the other half would receive the study agent in both sides of the brain, and the individuals conducting the study would know whether any given subject was receiving the study agent or a placebo.[11]

The principal investigator ("PI") of the experiment was originally Emad Eskandar, M.D.[12] The design and the informed consent forms were approved by the individual members of the institutional review board ("IRB").[13] Under federal regulations, institutional review boards review and approve human subject research.[14] The listed sponsor of the experiment was Neurologix.[15] Federal regulations define a "sponsor" of a clinical trial as a party that "takes responsibility for and initiates a clinical investigation."[16] One of the largest investors in Neurologix was Medtronic, which used the experiment to test its Acute Brain Infusion Delivery System ("ABID System"), an unapproved device that Medtronic hoped to bring to market.[17] The ABID System was to be used to deliver the genes directly into the brains of the human

[8] See Amended Complaint, ¶ 20.
[9] See Amended Complaint, ¶ 20.
[10] See Amended Complaint, ¶ 21.
[11] See Amended Complaint, ¶ 24.
[12] See Amended Complaint, ¶ 22.
[13] See Amended Complaint, ¶ 23.
[14] See, e.g., 45 C.F.R. § 46.101.
[15] See Amended Complaint, ¶ 25.
[16] See 21 C.F.R. § 312.3. In their proposed Second Amended Complaint, the Plaintiffs allege that a sponsor of a Gene Therapy trial must present its proposed study to the RAC, take authorship of the protocol, and represent that it will meet certain safety criteria.
[17] See Amended Complaint, ¶ 25.

subjects.[18] Dr. Eskandar and Neurologix chose Ziv Williams, M.D. of Harvard University to conduct the surgery using the ABID System.[19] Neurologix, Medtronic, Dr. Eskandar, the IRB members, and Dr. Williams formed the research enterprise for the experiment ("Research Enterprise").[20]

II.

When the experiment was first proposed to the Recombinant DNA Advisory Committee ("RAC"), the federal government body designated to oversee all Gene Transfer experiments, a member of the RAC warned that treatment in only one side of the brain was "handicapping."[21] Thus, the members of the Research Enterprise knew that the AAV carried genes, or what the Informed Consent Form called the "study agent," which had to be delivered in both sides of the brain or else the human subject could be left seriously debilitated.[22]

Prior to enrolling in the experiment, Mr. Zeman was provided with an Informed Consent Form. This Informed Consent Form did not mention the risk that the study agent might not be delivered into both sides of the brain; that the catheter in the ABID System might be misplaced or incorrectly placed; that a double dose of the study agent might result from such improper placement; and that there was a risk of "handicapping" from either a double dose on one side, or from a single dose on one side and no dose on the other side.[23] Furthermore, the Informed Consent Form did not mention that there was no radiologic or other procedure in the protocol designed to reliably confirm proper placement of the ABID catheters prior to infusion of the

[18] See Amended Complaint, ¶ 25.
[19] See Amended Complaint, ¶ 26.
[20] See Amended Complaint, ¶ 27. As noted in the Amended Complaint, Dr. Eskandar was later replaced by Dr. Flaherty. See Amended Complaint, ¶ 46.
[21] See Amended Complaint, ¶ 29.
[22] See Amended Complaint, ¶ 29.
[23] See Amended Complaint, ¶ 32.

study agent.[24] Additionally, the Informed Consent Form and the limited discussions that Dr. Eskandar had with Mr. Zeman were materially misleading and deceptive in several other respects: the procedure was represented to be therapeutic in nature rather than "a human experiment"; the risk of toxic effects associated with the virus vector was understated; Gene Transfer was represented to be a proven delivery device, rather than an unproven and high-risk procedure with consequences unknown to even the world's premier Gene Transfer scientists; the procedure was represented to be safe and effective; there was no disclosure with respect to prior animal studies; and there was no disclosure with respect to the financial conflicts of interest inherent in the experiment.[25] Relying on the representations made by the members of the Research Enterprise, Mr. Zeman signed the Informed Consent Form.[26]

On December 4, 2008, Mr. Zeman became the first human subject (at Massachusetts General or anywhere else) to have what was supposed to be bilateral Gene Transfer in the brain as a potential cure or therapy for Parkinson's.[27] Dr. Williams conducted the surgery with representatives of both Neurologix and Medtronic in the room.[28] (In the Plaintiffs' proposed Second Amended Complaint, which they will shortly be moving for leave to file, they allege that Dr. Kaplitt attended the surgery "as a Neurologix corporate representative." They further allege that, before the surgery, Dr. Kaplitt and Mr. Zeman shook hands and talked about Neurologix' discovery, and Dr. Kaplitt left the surgery halfway through, after the left side was completed, because the surgery was taking longer than he expected it to and he had a flight to catch.)

---

[24] See Amended Complaint, ¶ 33; see also Amended Complaint, ¶ 135(e) (alleging that "there was no radiologic or other procedure in the protocol designed to reliably confirm proper placement of the ABID catheters prior to infusion of the study agent"). In the Plaintiffs' proposed Second Amended Complaint, the Plaintiffs specifically allege that the protocol was flawed because it did not provide for intraoperative X-ray confirmation of catheter positions.

[25] See Amended Complaint, ¶ 34.

[26] See Amended Complaint, ¶ 35.

[27] See Amended Complaint, ¶ 36.

[28] See Amended Complaint, ¶ 37.

Contrary to the experiment's design and the RAC's warnings, the catheter component of the ABID System was not placed into each side of Mr. Zeman's brain; rather, the two catheters were both placed in the left side of his brain, delivering a double dose of the study agent only on the left side of the brain.[29] Shortly after the surgery, a CT scan clearly showed that the right catheter was misplaced into the left STN.[30] After the surgery was completed, the parties in the Research Enterprise, in violation of their ethical, legal, and regulatory obligations, willfully attempted to cover up what they knew to be a serious and catastrophic mistake.[31]

At first, Mr. Zeman was repeatedly told that the surgery went well; this was not true.[32] Approximately two weeks after the surgery, Mr. Zeman met with Dr. Williams, who advised Mr. Zeman that he only received the study agent on one side, the left, because there was "a kink" in the right-side catheter; this was not true either.[33]

In March 2009, Mr. Zeman and his wife returned for a follow-up visit.[34] Mr. Zeman was presented with another Informed Consent Form.[35] To his eye, the new form appeared identical to the one he had previously signed, save for a change in PI.[36] Mr. Zeman signed this form, not realizing that inserted in the document under "risks" was this sentence: "There is also a risk that the catheter … used in the surgery might be misplaced or incorrectly placed."[37]

Upon returning home, Mr. Zeman's dyskinesia (movement issues) began increasing and became more debilitating.[38] When Mr. Zeman returned to Boston for a follow-up visit, he was advised there was some improvement in motor skills, but only on the right side (which is

[29] See Amended Complaint, ¶ 38.
[30] See Amended Complaint, ¶ 39.
[31] See Amended Complaint, ¶ 40.
[32] See Amended Complaint, ¶ 41.
[33] See Amended Complaint, ¶ 42.
[34] See Amended Complaint, ¶ 46.
[35] See Amended Complaint, ¶ 47.
[36] See Amended Complaint, ¶ 47.
[37] See Amended Complaint, ¶ 48.
[38] See Amended Complaint, ¶ 49.

controlled by the left side of the brain).[39] During the visit, Mr. Zeman underwent PET scans, among other tests, and was given a phone number for Dr. Andrew Feigin, the individual who would be interpreting the PET scans.[40] When Mr. Zeman called the number, Dr. Feigin remarked, "So you're the guy who got the double dose of the gene on one side?" This was the first time Mr. Zeman learned that he had received a double dose of the study agent in his left STN.[41] When Mr. Zeman called Dr. Williams and asked about the possibility of a "double dose," Dr. Williams replied that he did not receive an extra dose because the right catheter had malfunctioned; nothing in the records, however, corroborates this claim.[42]

In July 2009, Dr. James Sutton, Mr. Zeman's physician, requested the medical records in an effort to determine why Mr. Zeman was deteriorating so rapidly, and how he could have received a double dose.[43] Massachusetts General provided a limited number of records.[44] Dr. Sutton advised Mr. Zeman to get the right STN done as soon as possible, as this was his best hope.[45] In January 2010, however, Mr. Zeman was advised he had developed a "slight" buildup of antibodies because of the mutated AAV virus, the Gene Transfer vector, and further advised that a second surgery could cause brain inflammation, encephalitis, and/or death.[46]

As a result of the infusion of a double dose of the study agent on only one side of the brain, Mr. Zeman has suffered and will continue to suffer severe and debilitating injuries, and owing to the mistake and the cover-up, Mr. Zeman has forever lost the possibility of having an infusion on the right side of his brain or of ever correcting the dose imbalance.[47]

---

[39] See Amended Complaint, ¶ 50.
[40] See Amended Complaint, ¶ 51.
[41] See Amended Complaint, ¶ 52.
[42] See Amended Complaint, ¶ 55.
[43] See Amended Complaint, ¶¶ 56-57.
[44] See Amended Complaint, ¶ 57.
[45] See Amended Complaint, ¶ 59.
[46] See Amended Complaint, ¶ 61.
[47] See Amended Complaint, ¶¶ 62- 63; see generally Amended Complaint, ¶¶ 15-66.

LEGAL ARGUMENT

1. Standards Governing 12(b)(6) Motions to Dismiss

Even following the issuance of Iqbal and Twombly, federal courts must continue to accept as true "all well-pleaded facts" (which include "either direct or inferential" factual allegations), analyze those facts "in the light most hospitable to the plaintiff's theory," and draw "all reasonable inferences for the plaintiff."[48]

2. Mr. Zeman has Stated a Negligence Claim Against Neurologix

In the Amended Complaint, Mr. Zeman alleges as follows:

> At all times, the Defendants, and each of them respectively, jointly, and severally, were charged with the professional responsibility of conducting an ethical experiment where risks did not greatly exceed benefits, of determining the universe of harm through proper preclinical animal studies, of properly conducting the informed consent process, of rendering proper care and treatment to Mr. Zeman, of properly and carefully designing and administering the experiment's protocol in a careful and prudent fashion, of assuring that proper care and attention were provided during all periods of time during which he remained under defendants' care and treatment, and of candidly and honestly advising him of the results and consequences of the experiment.[49]

In Count XI of the Amended Complaint, Mr. Zeman alleges that Neurologix was negligent in connection with the protocol and the informed consent process.[50]

Neurologix first argues that Mr. Zeman has failed to state a claim for negligence because the sponsor of a clinical trial owes no tort duty to a participant. In support of its argument, Neurologix relies upon an unpublished Massachusetts trial court decision and two decisions issued by other District Courts. These non-precedential cases are wrongly decided, inconsistent with Massachusetts law governing the imposition of a tort duty, and distinguishable.

---

[48] See, e.g., U.S. ex rel. Hutcheson v. Blackstone Medical, Inc., – F.3d – (1st Cir. 2011).
[49] See Amended Complaint, ¶ 28.
[50] See Amended Complaint, ¶¶ 131-137.

In order to prevail on a negligence claim, "a plaintiff must prove that the defendant owed the plaintiff a duty of reasonable care, that the defendant breached this duty, that damage resulted, and that there was a causal relation between the breach of the duty and the damage."[51] "A basic principle of negligence law is that ordinarily everyone has a duty to refrain from affirmative acts that unreasonably expose others to a risk of harm."[52] Beyond this, "[w]hether a duty exists is a question of common law, to be determined by 'reference to existing social values and customs and appropriate social policy.'"[53]

Further, "violations of a statute or regulations … may provide evidence of negligence" with regard to "all consequences that the statute … or regulation was intended to prevent."[54] 45 C.F.R. § 46.101, et seq. ("Common Rule") and 21 C.F.R. § 312.1, et seq. ("IND Regulations") were promulgated in order to prevent injury to participants in clinical trials. Thus, the tort duty of a member of the research enterprise is analyzed consistent with those federal regulations.[55] Indeed, "existing social values and … appropriate social policy" are reflected in those regulations, as well as the historical events leading to their enactment.

---

[51] See, e.g., Lev v. Beverly Enterprises-Massachusetts, Inc., 929 N.E.2d 303, 309 (Mass. 2010) (quoting Jupin v. Kask, 849 N.E.2d 829 (Mass. 2006)).

[52] Yakubowicz v. Paramount Pictures Corp., 536 N.E.2d 1067, 1070 (Mass. 1989); accord Remy v. MacDonald, 801 N.E.2d 260, 262-63 (Mass. 2004) (citing Restatement (Second) of Torts § 302) ("As a general principle of tort law, every actor has a duty to exercise reasonable care to avoid physical harm to others.").

[53] See Remy, 801 N.E.2d at 262 (quoting Cremins v. Clancy, 612 N.E.2d 1183 (Mass. 1993)).

[54] See, e.g., Berish v. Bornstein, 770 N.E.2d 961, 978-79 (Mass. 2004); Perry v. Medeiros, 343 N.E.2d 859, 862 (Mass. 1976).

[55] See Grimes v. Kennedy Krieger Inst. Inc., 782 A.2d 807 (Md. 2001) (recognizing a cause of action for negligence where the federal regulations governing human subject trials were violated); Daum v. Spinecare Medical Group, Inc., 52 Cal. App. 4th 1285 (1997) (holding that the federal regulations governing human subject trials were designed to prevent injury to participants in human research experiments, and that individuals participating "in clinical investigations are the intended beneficiaries of" those laws); Whitlock v. Duke University, 637 F.Supp. 1463 (M.D.N.C. 1986), aff'd, 829 F.2d 1340 (4th Cir. 1987).

After the Holocaust, a series of unprecedented war crimes trials took place in Nuremberg, Germany. The charges against the defendant physicians included acts performed under the guise of human experimentation that were actually taken in the reckless pursuit of scientific knowledge or for sadistic purposes. After 139 court sessions, the tribunal convicted sixteen defendants of war crimes against humanity and condemned seven to death. Though nothing else was required, the tribunal did far more. Holding that "certain basic principals must be observed in order to satisfy moral and legal concepts," the tribunal articulated what is now known as the Nuremberg Code. The very first principle provided as follows:

> The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the interventions of any elements of force, fraud, deceit, duress, over reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject, there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment. The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs, or engages in the experiment. It is a personal duty and responsibility, which may not be delegated to another with impunity.

(Emphasis added.)[56] In 1964, the World Medical Association adopted the Declaration of Helsinki, which set a worldwide minimal standard for human subject research. It provides, in pertinent part, as follows: "In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and

[56] See http://www.ushmm.org/research/doctors/ (last visited June 22, 2011).

society.[57] … In any research … , each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail."

In the 1970's, the National Commission for the Protection of Research Subjects in Biomedical and Behavioral Research issued the Belmont Report, which sets forth three principles to guide human subject research: respect for persons, which demands that researchers fully inform their subjects of all material information about the study and only then obtain their voluntary consent; beneficence, which prohibits any experiment where the risks are too great or outweigh the benefits; and justice, which requires the equitable selection of research subjects. These "serve as the foundation for the federal regulations governing human subject research."[58]

Consistent with the foregoing sources, the Common Rule and the IND Regulations impose significant and overlapping duties on the part of participants in the research enterprise.

Under the Common Rule, every IRB must ensure that risks to subjects are minimized through the use of "procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk."[59] Every IRB must further ensure that risks to subjects "are reasonable in relation to anticipated benefits."[60] IRB's are also responsible for reviewing and approving the informed consent document to be used in the study.[61] The Common Rule further provides that informed consent forms must provide an accurate explanation of the

---

[57] Neurologix argues that this tribunal "should be mindful that allowing Zeman's pending claims against Neurologix … would hinder a clinical study that offers a potential breakthrough in the treatment of Parkinson's disease." This self-serving assertion is both untrue (insofar as the trial will continue regardless of the outcome of this case) and in conflict with the principles that Neurologix, as a member of the Research Enterprise, is sworn to uphold.

[58] See, e.g., Danielle C. Beasley, Coupling Responsibility With Liability: Why Institutional Review Board Liability is Good Policy, 36 N. Ky. L. Rev. 45, 49 (2009).

[59] See 45 C.F.R. § 46.111(a)(1).

[60] See id. § 46.111(a)(2).

[61] See id. § 46.116.

purposes of the research and an accurate explanation of the risks of the research.[62] Under the IND Regulations, a principal investigator must, among other things, "comply with all requirements regarding the obligations of clinical investigators"; "personally conduct or supervise the … investigation"; "ensure that the requirements relating to obtaining informed consent … are met"; and "ensure that the requirements relating to … institutional review board review and approval … are met."[63] An investigator is also responsible for, among other things, "obtaining the informed consent of each human subject to whom the drug is administered."[64]

The IND Regulations define a "sponsor" of a clinical trial as the party that "takes responsibility for and initiates a clinical investigation."[65] Those regulations proceed to list some of a sponsor's additional duties: "selecting qualified investigators, providing them with the information they need to conduct an investigation properly, ensuring proper monitoring of the investigation(s), ensuring that the investigation(s) is conducted in accordance with the general investigational plan and protocols ... , and ensuring that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug."[66] A sponsor that discovers that an investigator is not acting in accordance with any of the regulations governing clinical trials is obligated to "promptly" ensure compliance or suspend the study.[67] In essence, then, a sponsor's duties are coextensive with the duties incumbent upon the principal investigator. Indeed, the FDA believes that a sponsor can be held liable for negligence: the Common Rule provides that no informed consent form "may include any exculpatory language through which the subject … release[s] … the sponsor … from liability for negligence."[68]

---

[62] See id.
[63] See 21 C.F.R. § 312.53.
[64] See id. § 312.60.
[65] See id. § 312.3.
[66] See id. § 312.50.
[67] See id. § 312.56(b).
[68] See 45 C.F.R. § 46.116.

In Suthers v. Amgen, the New York District Court case that Neurologix relies upon, the plaintiffs, participants in an aborted clinical trial of a potential cure for Parkinson's, were "alleging no claim that the product was negligently designed or manufactured or that the sponsor failed to exercise reasonable care in warning plaintiffs."[69] Rather, the plaintiffs alleged the opposite: the study drug was beneficial to them, and the sponsor had breached its fiduciary duty in terminating the trial and refusing to allow the participants access to the study drug on a compassionate-use basis.[70] The trial court held that, under the facts and circumstances of the case, the sponsor had no such duty to plaintiffs, particularly in light of the promises made to them by the principal investigator without the sponsor's authority. The facts of Suthers are completely distinguishable and its holding is limited: the court did not hold that a sponsor never has a tort duty toward a participant.[71] Indeed, the federal regulations expressly state otherwise. Why would the regulations preclude language in an informed consent document exculpating a sponsor from a negligence claim if the sponsor could never be held liable for negligence?

In Darke, the unpublished Massachusetts case that Neurologix relies upon, the plaintiffs filed, among other claims, a negligence claim against the sponsor of a Gene Transfer trial.[72] The trial court dismissed that claim without considering the majority of the regulations referenced above or the fact that the sponsor of a Gene Transfer trial must present its proposed study to the RAC, take authorship of the protocol, and represent that it will meet certain safety criteria.[73] In Kernke v. The Menninger Clinic, Inc., the Kansas District Court case relied upon by Neurologix, the trial court rejected the plaintiff's claims that the sponsor of a trial was negligent in failing to

[69] See Suthers v. Amgen, 441 F. Supp. 2d 478, 488-89 (S.D.N.Y. 2006).
[70] See id.
[71] See Suthers, 441 F. Supp. 2d at 489-90.
[72] See Darke v. Estate of Isner, No. 022194E, 2005 WL 3729113 at *14 (Mass. Super. November 22, 2005).
[73] See id.

determine whether the benefits of the study outweighed the risks to him, failing to secure informed consent, and failing to "supervise [him] while he participated in the study."[74]

In determining that no tort duty existed, all three trial courts failed to analyze both the primary source documents leading up to regulation of clinical trials in the United States (which make clear that the "duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs, or engages in the experiment") and the overlapping responsibilities of sponsors, principal investigators, and internal review boards embodied in the Common Rule and the IND Regulations. These responsibilities overlap all the more in the Gene Transfer context, where the sponsor of a Gene Transfer trial appears before the RAC and makes representations about safety.[75] Holding that a study sponsor has a tort duty to study participants is consistent with "existing social values and customs and appropriate social policy."

Neurologix argues that "[s]trong public policy reasons support shielding sponsors from any duty involving the informed consent." In so arguing, Neurologix ignores both 21 C.F.R. § 312.56(b) and the history behind that regulation, including the Nuremberg Code, which provides that "each individual who initiates,[76] directs, or engages in the experiment" has a duty to obtain informed consent. Neurologix next argues that to "superimpose a duty on the sponsor would create a scenario in which sponsors may feel compelled to involve themselves in, and perhaps override, the sacrosanct doctor-patient relationship." This argument ignores the order of operations in a clinical trial: both the protocol and the informed consent documentation are authored, revised, and approved prior to the enrollment of subjects in a study.[77]

Neurologix concludes by contending that, even if it had a duty to Mr. Zeman, it did not breach that duty because his "injuries were caused by a surgical error … ." In so arguing,

---

[74] See Kernke v. The Menninger Clinic, Inc., 173 F. Supp. 2d 1117 (D.Kansas 2001).
[75] This allegation is set forth in the proposed Second Amended Complaint.
[76] A sponsor is the party that "initiates a clinical investigation." See 21 C.F.R. § 312.3.
[77] See generally 45 C.F.R. § 46.101, et seq.; 21 C.F.R. § 312.1, et seq.

Neurologix ignores Mr. Zeman's allegations that the informed consent process for which Neurologix was jointly responsible[78] was flawed, and Neurologix' conduct following the catheter misplacement (including its complicity in the cover-up, which served to delay and then eliminate the possibility of a follow-up surgery) ran contrary to its obligations under the applicable federal regulations. Neurologix further ignores the Plaintiffs' allegation that "there was no radiologic or other procedure in the protocol designed to reliably confirm proper placement of the ABID catheters prior to infusion of the study agent."[79] This flaw in the protocol caused and/or contributed to what occurred (i.e., if the protocol had called for a post-insertion but pre-infusion radiograph, this incident would not have occurred, or may have been less likely to occur). Neurologix cannot simply hide behind the principal investigator, as it attempts to do. Its motion to dismiss Count XI, for negligence, must be denied.

3. Mr. Zeman has Stated a Products Liability Negligence Claim Against Neurologix

21 U.S.C. § 360k, a section of the Medical Device Amendments to the Food, Drug and Cosmetic Act ("MDA"), provides that no state may, "with respect to a device intended for human use," impose any requirement that is "different from, or in addition to, any requirement of the Food, Drug and Cosmetic Act … which relates to the safety or effectiveness of the device."[80]

In Riegel v. Medtronic, Inc., the Supreme Court was asked to decide whether 21 U.S.C. § 360k preempted the plaintiff's design defect and breach of warranty claims.[81] The FDA had granted pre-market approval (when abbreviated, "PMA") to the manufacturer of the allegedly

[78] See 21 C.F.R. § 312.56(b) (providing that, if a sponsor learns that a principal investigator has failed to comply with any regulation governing human subject research, which by definition includes 21 C.F.R. § 312.60, the regulation requiring a principal investigator to obtain a subject's informed consent, the sponsor must take action).

[79] See Amended Complaint, ¶ 135(e).

[80] 21 U.S.C. § 360k(a).

[81] See Riegel v. Medtronic, Inc., 552 U.S. 312, 320-21, 326, 327-330 (2008).

defective device, a balloon catheter.[82] This catheter was a "Class III" device that had received the FDA's highest level of oversight during the PMA process.[83]

The Court first noted that the FDA on average spends 1,200 hours on each PMA application. The Court then noted that the MDA requires the FDA to "weig[h] any probable benefit to health from the use of the device against any probable risk of injury or illness from such use" prior to granting approval.[84] The Court further noted that, after approval, "the MDA forbids the manufacturer to make, without FDA permission, changes in design specifications, manufacturing processes, labeling, or any other attribute … ."[85]

In resolving the issue of whether the plaintiff's claims were preempted, the Court formulated the following two-pronged inquiry: (1) "whether the Federal Government has established requirements applicable to" the catheter; and (2) whether the "common-law claims are based upon [state] requirements with respect to the device that are 'different from, or in addition to' the federal ones, and that relate to safety and effectiveness."[86] With regard to the first prong, the Court found that the PMA process imposed federal requirements applicable to the catheter because pre-market approval is granted "only after [the FDA] determines that a device offers a reasonable assurance of safety and effectiveness" and because "the FDA requires a device that has received pre-market approval to be made with almost no deviations from the specifications in its approval application."[87] The Court proceeded to hold that the imposition of tort duties "would be pre-empted by federal requirements specific to a medical device."[88]

---

[82] See id.
[83] See id.
[84] See id. at 318-19 (citing 21 U.S.C. § 360c(a)(2)(C)).
[85] See id.
[86] See id. at 322 (citing 21 U.S.C. § 360k(a)).
[87] See id. at 323.
[88] See id. at 323-24.

The Court was careful to note that § 360k "does not prevent a State from providing a damages remedy for claims premised on a violation of FDA regulations," as "the state duties in such a case 'parallel,' rather than add to, federal requirements."[89]

In Count XII, for products liability, Mr. Zeman alleges that the ABID System was defectively designed and manufactured in violation of the Food, Drug and Cosmetic Act as well as the "terms, conditions, standards and specifications of the Investigational Device Exemption … secured [through] the Food and Drug Administration's Premarket Approval Process … ."[90] In its memorandum of law, Neurologix argues that Mr. Zeman's claims are preempted by the MDA and Mr. Zeman's "parallel" claims are insufficiently pled. Neither argument holds water.

To begin, no aspect of Mr. Zeman's manufacturing defect claims are preempted by the MDA. In Riegel, the Court had no occasion to consider whether the plaintiff's manufacturing defect claims were preempted.[91] The fact that pre-market approval "requires a device … to be made with almost no deviations from the [approved] specifications" strongly suggests that manufacturing defect claims, which are premised upon a deviation from approved specifications, are not preempted by the MDA. Indeed, in Hofts v. Howmedica Osteonics Corporation, the United States District Court for the Southern District of Indiana engaged in a lengthy analysis of Riegel and concluded that manufacturing defect claims are not preempted by the MDA.[92] In this case, as in Hofts, "it is clear that [the plaintiff] bases his tort claims on his allegations that [the manufacturer] failed to meet the FDA's requirements, not on allegations that [the manufacturer] failed to depart from or exceed those requirements," and a jury "could find that [the manufacturer] breached the duty of care it owed … by failing to adhere to … manufacturing

[89] See id. at 330.
[90] See Amended Complaint, ¶¶ 138-146.
[91] See Riegel, 552 U.S. at 312-13.
[92] See Hofts v. Howmedica Osteonics Corporation, 597 F. Supp. 2d 830 (S.D.Ind. 2009).

requirements without imposing different or additional requirements."[93] Similarly, because the ABID System was manufactured pursuant to an investigational device exemption and has not received pre-market approval, Mr. Zeman's design defect claims are not pre-empted.

Furthermore, Mr. Zeman's "parallel" claims have been pled with adequate specificity. As stated above, those claims are premised upon the allegation that the ABID System was defectively designed and manufactured in violation of the Food, Drug and Cosmetic Act, as well as the "terms, conditions, standards and specifications of the Investigational Device Exemption" secured through the PMA process.[94]

In Burgos v. Satiety, Inc., the plaintiff alleged that the defendant, the manufacturer of a device that caused injury during a clinical trial, violated the "terms, conditions, standards and specifications of the IDE secured by Satiety from the Food and Drug Administration's pre-market approval process."[95] The United States District Court for the Eastern District of New York held that the foregoing allegations were sufficient to state a claim against the defendant manufacturer.[96] The court proceeded to observe that, even though those allegations were "almost entirely devoid" of facts, this was understandable:

> [The plaintiff] does not allege how the … device's manufacture violated the IDE, nor does she specify the terms, conditions, standards, or specifications that she claims were violated. However, at this stage of the proceedings she cannot reasonably be expected to do so, because the information she requires to provide the requisite degree of specificity—the IDE documentation submitted … to the FDA—is confidential and not available to the public. See 21 C.F.R. § 812.38. If she had the same information that [the defendant] has, she might well be able to specifically

[93] See id.; accord Carson v. Depuy Spine, Inc., 365 Fed. App'x 812 (9th Cir. 2010); Warren v. Howmedica Osteonics Corporation, No. 4:10 CV 1346, 2011 WL 1226975 (E.D.Mo. March 29, 2011) (holding that manufacturing defects are not covered by Riegel).

[94] See Amended Complaint, ¶¶ 138-146.

[95] See Burgos v. Satiety, Inc., No. 10–CV–2680, 2011 WL 1327684 at *2 (E.D.N.Y. April 5, 2011) (alterations omitted). In its memorandum of law, Neurologix cited an earlier opinion in this very case without disclosing the existence or holding of this opinion.

[96] See id. at *3.

> allege ways in which [the defendant] was negligent in its manufacture of the … device used in her procedure. … [The plaintiff's] pleadings are entitled to [a] liberal reading … . Although the amended complaint is of necessity somewhat bare-bones, [the plaintiff] has diligently alleged as many facts as she can at this point.[97]

In the case of In re Medtronic, Inc. Sprint Fidelis Leads Products Liability Litigation, Judge Melloy, in a partial concurrence and dissent, observed that plaintiffs alleging "parallel" claims based on a violation of a manufacturer's agreement with the FDA often have no access to the agreements that would provide factual specificity because those agreements are confidential and available only to the defendants and the FDA.[98] Judge Melloy observed that Twombly "must be applied in a practical manner that recognizes the parties' relative access to information necessary to articulate claims with specificity."[99] He proceeded to note, "If plaintiffs must allege that the defendant violated a particular FDA-approved specification before discovery, then it is difficult to appreciate how any plaintiff will ever be able to defeat a Rule 12(b)(6) motion."[100]

In Bausch v. Stryker Corp., the Seventh Circuit adopted Judge Melloy's concurrence. The court held that, in assessing whether a complaint passes muster under Iqbal and Twombly, "district courts must keep in mind that much of the product-specific information about manufacturing needed to investigate such a claim fully is kept confidential by federal law" and "discovery is necessary before a plaintiff can fairly be expected to provide a detailed statement of the specific bases for [his or] her claim."[101]

---

[97] See id. at *4.

[98] See In re Medtronic, Inc. Sprint Fidelis Leads Prods. Liab. Litig., 623 F.3d 1200 (8th Cir. 2010) (Melloy, J., concurring in part and dissenting in part).

[99] See id.

[100] See id. The majority opinion was largely in accordance with this view. See id.

[101] See Bausch v. Stryker Corp., 630 F.3d 546 (7th Cir. 2010); accord Hofts, 597 F. Supp. 2d at 838 (observing that "[m]anufacturing defect claims are not subject … to the 'particularity' pleading requirements of Rule 9" and further observing that requiring specificity in this context represents an "unusually stringent application of Twombly and Rule 8 of the Federal Rules of Civil Procedure at the motion to dismiss stage").

Any contrary cases cited by Neurologix are wrongly decided and inconsistent with both the notice pleading requirements of the Federal Rules and the realities of the framework governing the investigational drug exemption and pre-market approval processes. Those decisions read out of Riegel the opportunity to pursue a claim that parallels FDA regulations. When Mr. Zeman requested his medical records, he was told that they were "confidential study records."[102] Neither Neurologix or Medtronic would have turned over the device at issue, or the documents generated in connection with the IDE. Only through discovery can counsel further develop the claim, including the claim as to how specifically the ABID System was defective.[103]

4. Mr. Zeman has Stated a Breach of Implied Warranty Claim Against Neurologix

In Massachusetts, a strict liability claim takes the form of a claim for breach of the implied warranty of merchantability.[104] In 1983, the Supreme Judicial Court held that, "as a matter of social policy, the warranty of merchantability imposes a special responsibility on the seller toward any member of the consuming public who may be injured by its product."[105] Three years later, in Mason v. General Motors Corp., the Supreme Court rejected a breach of warranty suit brought by the heirs of an individual who died while test-driving a Corvette on the ground the decedent had not purchased the allegedly defective product.[106] Two years later, in Colter v. Barber-Greene Co., the Supreme Judicial Court, implicitly recognizing the wisdom of the dissent in Mason, allowed an employee injured by a machine purchased by his employer to recover on a

[102] See Amended Complaint, ¶ 56.

[103] Contrary to the argument that the "Amended Complaint unequivocally alleges that there was no defect in the ABID System," and that "surgical misuse of the ABID System was the sole cause of … injuries," the Amended Complaint contains numerous allegations that the ABID System was defective and caused Mr. Zeman's injuries. See Amended Complaint, ¶¶ 138-146.

[104] See, e.g., Haglund v. Phillip Morris Corp., 847 N.E.2d 315, 321 (Mass. 2006); Cigna Ins. Co. v. Oy Saunatec, Ltd., 241 F.3d 1, 15 (1st Cir. 2001) ("Actions under Massachusetts law for breach of the implied warranty of merchantability are the functional equivalent of strict liability in other jurisdictions.").

[105] See id. (internal alterations omitted) (citing Correia v. Firestone Tire and Rubber Co., 446 N.E.2d 1033 (Mass. 1983)).

[106] See Mason v. General Motors Corp., 490 N.E. 2d 437 (Mass. 1986).

breach of warranty theory.[107] Thus, under Colter, in order to recover on a breach of warranty theory, a plaintiff does not need to personally purchase the product at issue.

Viewing the Amended Complaint in the light most favorable to Mr. Zeman, a party may have provided consideration, monetary or otherwise, for the ABID System.[108] The Plaintiffs should be allowed to conduct discovery regarding the consideration provided for the transfer of ownership of the device. Neurologix' motion to dismiss Count XIII must be denied.[109]

CONCLUSION

For the foregoing reasons, the Motion must be denied.

Dated: June 24, 2011

Respectfully submitted,

/s/ Scott E. Charnas

Scott E. Charnas, BBO #081240
Charnas Law Firm, P.C.
66 Long Wharf
Boston, MA 02110
Telephone: 617-557-4700
Facsimile: 617-557-9199
Email: scharnas@charnaslawfirm.com

OF COUNSEL:

Alan C. Milstein, Esquire
Sherman, Silverstein, Kohl, Rose & Podolsky, P.A.
308 Harper Drive, Suite 200
Moorestown, NJ 08057
Telephone: 856-662-0700
Facsimile: 856-662-0165
Email: amilstein@shermansilverstein.com

[107] See Colter v. Barber-Greene Co., 525 N.E.2d 1305 (Mass. 1988).

[108] A "sale" can be accomplished by the exchange of non-monetary consideration. See, e.g., Nemours & Co. v. Kaufman & Chernick, Inc., 148 N.E.2d 634 (Mass. 1958).

[109] Moreover, with regard to this claim, the Plaintiffs should be given a chance to develop through discovery evidence relating to a choice of law analysis. Mr. Zeman is a citizen of California; Neurologix is based in New Jersey. Beginning in 1976, the Supreme Judicial Court moved towards the approach that the state in which a tort occurs is not necessarily the state whose law controls. See Pevoski v. Pevoski, 358 N.E.2d 416 (Mass. 1976).

CERTIFICATE OF SERVICE

I, Scott E. Charnas, hereby certify that, on June 24, 2011, I served a copy of this Plaintiffs' Memorandum of Law in Opposition to Defendant Neurologix, Inc.'s Motion to Dismiss (filed through the ECF system) electronically to the registered participants as identified in the Notice of Electronic Filing (NEF) and by sending paper copies via first class U.S. mail, postage prepaid, to those indicated as non-registered participants.

/s/ Scott E. Charnas
Scott E. Charnas